

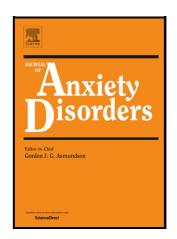
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Tonic immobility is associated with posttraumatic stress symptoms in healthcare professionals exposed to COVID-19-related trauma

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Title: Tonic immobility is associated with posttraumatic stress symptoms in healthcare professionals exposed to COVID-19-related trauma

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Abstract

The Coronavirus Disease 2019 (COVID-19) pandemic has exposed healthcare workers (HCW) to traumatic situations that might lead to the development of posttraumatic stress disorder (PTSD). An important vulnerability factor for PTSD is the peritraumatic tonic immobility (TI) reaction, an involuntary and reflexive defensive response evoked by an intense and inescapable threat. TI is largely understudied in humans and has not been investigated during trauma related to COVID-19. For HCW, the pandemic context might be experienced as an intense and potentially inescapable threat, i.e., an overwhelming situation. Here, we investigated if TI response occurred during traumatic events related to the pandemic and its association with posttraumatic stress symptoms (PTSS). An online survey of 1001 HCW investigated COVID-19-related traumatic experiences, TI and PTSS. TI was reported for all types of traumatic events, and multivariate regression models revealed that TI was significantly associated with PTSS severity. HCW who reported high TI scores exhibited an

increase of 9.08 times the probability of having a probable diagnosis of PTSD. Thus, TI was evoked by pandemic-related traumatic situations and associated with PTSS severity and higher odds of a PTSD diagnosis. Tonic immobility occurrence should be screened, and psychoeducation about its reflexive biological nature should be introduced.

Keywords:

COVID-19, healthcare worker, tonic immobility, posttraumatic stress disorder

1. Introduction

Since the Coronavirus Disease 2019 (COVID-19) pandemic has resulted in an unprecedented situation, threatening global health, urgent and necessary actions have needed to be taken by governments to address the crisis (WHO, 2020; Cucinotta & Vanelli, 2020). Although many countries have designed healthcare strategies, they have seen their health systems nearly or actually collapse, forcing healthcare workers (HCW) to manage adverse situations encompassing physical and psychological demands (Nguyen et al., 2020; Johnson et al., 2020). The situation was particularly dramatic in Brazil, which had one of the worst global responses to the pandemic (Lancet, 2020), surpassing 600,000 deaths at the time this paper was written (CSSE, 2020). Additionally, COVID cases were still increasing when many Brazilian states lifted restrictions on businesses and shared spaces, increasing pressure on the healthcare system. This dramatic situation imposed by the pandemic forced HCW to cope with sleep deprivation, pressure to act without needed training, heavy workloads, and lack of personal protective equipment (PPE). All these factors have been suggested as important stressors that could impact their mental health (d'Ettorre et al., 2021; Nguyen et al., 2020; Yin et al., 2020; Paiano et al., 2020). Additionally, HCW were exposed to the fear of being contaminated and the fear of contaminating family members or losing someone close to them, such as a coworker or family member (Rose, 2020; Robles et al., 2020), among other COVID-19-related potentially traumatic events.

One of the worst outcomes of the exposure to potentially traumatic events is the development of posttraumatic stress disorder (PTSD). This potentially chronic impairing disorder is characterized by intrusive memories, avoidance, negative alterations in mood and cognition, and hyperarousal after exposure to actual or threatened death, serious injury, or sexual violence (APA, 2013). Experiencing work-related potentially traumatic events can trigger posttraumatic stress symptoms (PTSS) (APA, 2013; Johnson et al., 2020; d'Ettorre et al., 2021; Benfante et al., 2020). Therefore, it is not surprising that the prevalence rates of PTSD among healthcare professionals working with COVID-19 patients may reach 56.6% (d'Ettorre et al., 2021). Considering that the COVID-19 pandemic is still ongoing, it is indispensable to comprehend the risk factors that can contribute to the development or severity of PTSD in healthcare professionals.

A very important but understudied vulnerability factor for PTSD is peritraumatic tonic immobility. Tonic immobility (TI) consists of an involuntary and reflexive defensive response evoked by an intense and inescapable threat and is characterized by reversible

profound immobility, analgesia, and relative unresponsiveness to external stimulation. This defensive response has been extensively described in nonhuman species and is considered the last anti-predator resort when survival is extremely threatened (Ratner, 1967; Marks, 1987; Volchan et al., 2017). TI may increase the chances of survival as the cessation of preyspecific responses, such as struggling and vocalizations, reduces the chances of a predator attack (Marks, 1987). Until more recently, this defensive response in humans was less studied, and its initial descriptions employed systematic retrospective reports from female victims of sexual assault (Bovin et al., 2008; Fusé et al., 2007; Galliano et al., 1993; Heidt et al., 2005; Humphreys et al., 2010; Kalaf et al., 2017). Using a similar approach, studies based on systematic retrospective reports from our group have expanded knowledge about adverse situations associated with TI as a defensive response and indicate that it occurs, for example, after urban violence-related traumatic events and in both genders (Fiszman et al., 2008; Kalaf et al., 2015; Maia et al., 2015; Marx et al., 2008; Reichenheim et al., 2014; Portugal et al., 2012; Magalhães et al., 2021). More importantly, we conducted experiments using postural and cardiac recordings that support the presence of TI in human beings (Alves et al., 2014; Norte et al., 2019; Volchan et al., 2011, 2017). Collectively, these studies suggest that the occurrence of TI in situations of intense threat in humans is not uncommon. Crucially, the occurrence of this defensive reaction has been consistently associated with PTSD severity. Fiszman et al. (2008) reported a high prevalence of peritraumatic TI in patients with PTSD. More importantly, this study highlights that TI occurrence was associated with a poorer response to pharmacological treatment for PTSD when compared to that of patients without TI. Rocha-Rego and collaborators (2009) investigated the role of TI and more conventional peritraumatic reactions, e.g., dissociation and panic, as predictors of PTSD symptoms severity and observed, in a sample of PTSD patients, that TI was the only significant predictor of PTSD symptoms severity after controlling for potential confounders. Moreover, Lima et al. (2010) showed that, when compared to other peritraumatic responses, TI was the most important predictor of a poor response to PTSD treatment (Lima et al., 2010). TI has been also associated with an increased severity of symptoms in nonclinical samples (Portugal et al., 2012; Maia et al., 2015; Kalaf et al., 2015; Magalhães et al., 2021). Thus, TI occurrence seems to be a significant vulnerability factor for PTSD, although the exact mechanisms underlying the TI-PTSD association is not known.

However, until now, this peritraumatic reaction was not a major concern of scientific research in adverse epidemic/pandemic contexts. To the best of our knowledge, no studies have investigated the occurrence of TI as a response during trauma related to COVID-19. In the COVID-19 pandemic, healthcare professionals are constantly faced with not only the potential death of coworkers and/or family members but also the fear of being infected and infecting others. Given that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is contagious and considered potentially lethal (Hung, 2020; Harfouch et al., 2021) and responsible for the death of more than six hundred thousand people in Brazil (https://covid.saude.gov.br/), it is conceivable that for HCW the pandemic context might represent an overwhelming threat. The inevitable encounter with this type of danger might be experienced as an intense, potentially inescapable and very close threat, which are threat

characteristics known to evoke the TI response. Considering the deleterious impacts of tonic TI, particularly its association with PTSD severity and that its occurrence has been described in other professionals, such as police officers and rescuers (Maia et al., 2015), it is urgent to investigate whether this peritraumatic defensive response occurred in HCW during traumatic events related to the COVID-19 pandemic and its consequences for their mental health.

The aim of this study was to investigate the occurrence of the peritraumatic tonic immobility response during traumatic events specifically related to the pandemic and its association with PTSD symptomatology. To assess this issue, participants answered a questionnaire that investigated potential traumatic situations experienced during the COVID-19 pandemic qualifying for the DSM-5 PTSD criterion A. TI reaction and PTSD symptomatology were reported based on the event identified as the most traumatic in the COVID-19 experiences questionnaire. Considering that many situations during the adverse pandemic context might have been perceived as overwhelming and inescapable threats, we hypothesized that high levels of tonic immobility response would be reported by participants during traumatic events related to the COVID-19 pandemic and that these experiences would be strongly linked to PTSD symptom severity. During the data collection of this research, Brazil registered 4.5 million cases of COVID-19 and more than 136,000 deaths (www.worldometers.info/coronavirus/country/brazil/), and no effective vaccine was available to treat COVID-19.

2. Methods

2.1 Ethical concerns

This study was approved by the Ethics Review Board of the Universidade Federal Fluminense and National Research Ethics Commission (CONEP) under process number CAAE 31044420.9.0000.5243. All methods were carried out following relevant guidelines and national regulations. All participants agreed to participate in the survey voluntarily and provided informed consent.

2.2 Study design and recruitment procedure

This study is part of the PSIcovidA project, an ongoing project with a longitudinal design developed to investigate the effects of the pandemic on the mental health of professionals working in hospitals or urgent care units and acting directly or indirectly in the fight against COVID-19. The data reported here are based on the first wave of the study and were collected over three months, between June 12th, 2020, and September 19th, 2020.

The data were collected by a convenience snowball sampling technique geared toward professionals working in different healthcare setups or in urgent care units in different states of Brazil, including private and public hospitals, public healthcare clinics and other healthcare facilities in which COVID-19 patients were treated. All questionnaires were administered online and were sent by e-mail, via WhatsApp Messenger (WhatsApp Inc, Mountain View, CA, USA) and posted on social media. To increase visibility and enhance

participant recruitment, we created a social media account (Instagram: @projetopsicovida) and a web page (www.psicovida.org) for the project, which also contained a link to the online survey. Additionally, the associations of all major health worker groups and professional council boards in Brazil were contacted to publish an invitation with the link to answer the online survey on their websites and Instagram for potential participants. Moreover, interviews in Brazilian media about the study were carried out to invite people who worked in a hospital environment or emergency units to participate.

2.3 Participants

In total, 1,843 respondents accessed and completed the web survey. The inclusion criterion was being a healthcare worker, which is defined here as professionals working in hospitals or emergency care units, e.g., physicians, nurses, psychologists and administrative personnel, yielding a sample of 1399 participants. The exclusion criteria were not having experienced a traumatic event related to the COVID-19 pandemic situation (n= 220) and failing to fully complete the questionnaire battery (n= 178). The occurrence or absence of traumatic events related to COVID-19 was evaluated by a questionnaire containing several items describing potentially traumatic situations according to DSM-5 criteria A for PTSD (see Measures section below). The final sample consisted of 1001 respondents from all 26 different states in Brazil. Figure 1 shows a flowchart presenting the steps followed to obtain the final sample. Our sample presented a mean age of 40.4 years (SD = 10.7, 19-83 years), with a large portion of the respondents living in Rio de Janeiro (62%) and the majority of respondents consisting of women (n=765, 76.5%). Estimates by the National Council of Municipal Health Secretariats (CONASEMS), based on data from the Brazilian Institute of Geography and Statistics (IBGE), indicate that women represent 65% of the more than six million professionals working in the public and private health sector at all levels of care complexity (CONASEMS, 2020). The characteristics of this sample are described in Table 1.

2.4 Measures

2.4.1 Sociodemographic questionnaire

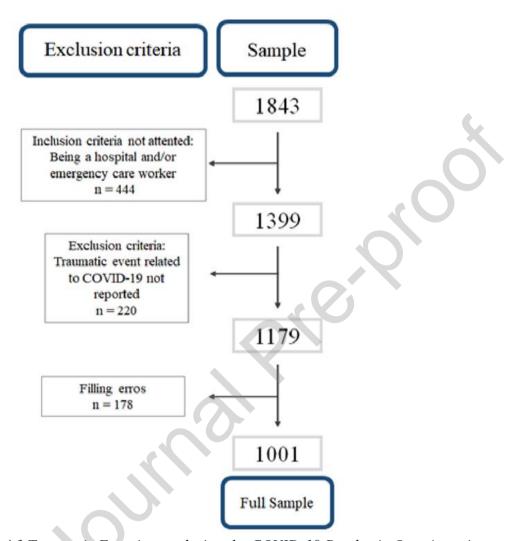
A series of survey questions inquired about gender, age, ethnic group, state of residence, occupation, type of health institution (public, private or both), monthly family income, and the number of people living with the respondent.

2.4.2. Availability of personal protective equipment (PPE)

This questionnaire investigated the availability of PPE and stress levels when it was not duly delivered. This item was investigated and answered through the following question: "Following pandemic start, have you received personal protective equipment: Sufficiently/Variably, sometimes yes, sometimes no/Unsatisfactorily, there is always some PPE missing/Rather not answer". Participants who answered "Variably" or "Unsatisfactorily" were referred to answer the second question regarding PPE availability: "Regarding the previous question, if you have not received PPE satisfactorily, indicate, on a scale from 1 to

10, your stress level due to not receiving it properly". For the purposes of this study, only the first question was used.

Figure 1: Flowchart of sample inclusion and exclusion criteria



2.4.3 Traumatic Experiences during the COVID-19 Pandemic Questionnaire

This questionnaire was composed of seven items that investigated traumatic situations experienced during the COVID-19 pandemic. All the items are in accordance with DSM-5 criteria A for the development of PTSD, which involve direct or indirect exposure to death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence. The items were as follows: (1) personally witnessing the death of a patient due to COVID-19; (2) personally witnessing the death of a family member or coworker due to COVID-19; (3) learning, through others, about the death of a family member or a coworker due to COVID-19; (4) experiencing the imminent risk of death of a family member or coworker due to COVID-19; (5) being exposed to critically ill patients infected with COVID-19 whose lives were in danger; (6) being infected with COVID-19; and (7) believing or having confirmation that one may have transmitted the virus to someone very close (coworker, partner, friend or family). For each item, participants were asked if they had experienced the given situation

and answered "yes or no." At the end of the questionnaire, an index trauma question asked about participants' worst experience among the seven items listed above and how long ago the event had occurred (less or more than one month). The questionnaire is presented in Appendix I in the supplemental material.

The content validity of the Traumatic Experiences during the COVID- 19 Pandemic Questionnaire was examined qualitatively and relied on the subjective judgments of PTSD experts' (two psychiatrists and one psychologist), always observing the DSM-5 criteria for PTSD diagnostics.

2.4.4. Posttraumatic Stress Disorder Checklist for the DSM-5 (PCL-5)

Developed by the National Center for PTSD in accordance with the DSM-5 (APA, 2013), the PCL-5 assesses posttraumatic stress symptoms (Weathers et al., 2013). The 20-item self-report questionnaire was translated and adapted to Portuguese, and each item was rated on a 5-point Likert scale (from 0= "Not at all" to 4="Extremely"). It measures the four clusters of PTSD symptoms: intrusion, avoidance, negative alterations in cognition and mood, and alterations in arousal and reactivity. Symptom severity can be calculated by summing the items in each of the four clusters or summing all 20 items. For the purposes of this study, a total score was selected to be considered in the analysis of symptom severity, which ranges from zero to 80 points. Participants were asked to choose the worst event reported in the Traumatic Experiences during the COVID-19 Pandemic Questionnaire and indicate how each item of the PCL-5 bothered them in the last month. For the analysis in which participants were divided into two groups, with or without a possible PTSD diagnosis, we used a cutoff PCL score of 36 or higher, as the literature suggests that this cutoff has the best diagnostic performance for predicting a diagnosis of PTSD (Pereira-Lima et al., 2019).

The PCL-5 has been assessed in different cultural contexts and samples. Its psychometric properties have presented strong convergent and discriminant validity, very good to high test-retest reliability, and satisfactory to high internal consistency (Blevins et al., 2015; Ashbaugh et al., 2016; Sveen et al., 2016). We used the cross-cultural adaptation for the Brazilian context proposed by Lima et al. (2016).

Internal consistency for the present study, assessed by Cronbach's alpha, was high for the whole scale (0.947), as well as for the theoretical dimensions of the DSM 5 (criterion B=0.897, criterion C=0.799, criterion D=0.898 and criterion E=0.834).

2.4.5 Tonic Immobility Scale (TIS)

The TIS is a self-report measure developed to assess the presence and severity of the features and components of tonic immobility. Its original version has ten items rated on a 7-point Likert scale ranging from 0 to 6 (Fusé et al., 2007). A validated Brazilian version was refined by Reichenheim et al. (2014), resulting in a one-factor solution and a reduced number of items. In the present study, we employed this six-item version, with scores ranging from 0-36. Participants also adhered to the TIS based on the worst event reported on the Traumatic

Experiences during the COVID-19 Pandemic Questionnaire and rated the degree to which they: (1) felt unable to move even though not restrained during the event; (2) felt unable to call out or scream during the event; (3) felt numb or no pain during the event; (4) felt cold during the event; (5) felt feelings of fear/panic during the event; (6) and felt detached from themselves during the event.

The internal consistency for the present study assessed by Cronbach's alpha was 0.87.

2.5 Procedures

Participants interested in the study accessed the web survey through a link that directed them to the Google Forms platform, in which the protocol was hosted. An initial text presented the general purposes of the research and asked if the respondent was a hospital or emergency healthcare worker. An affirmative answer directed participants to read the consent terms, which guaranteed anonymity and freedom to end participation. Those who provided consent were directed to answer the questionnaire battery. The questionnaire protocol included a sociodemographic survey, followed by items asking about the availability of PPE, the Traumatic Experiences during the COVID-19 Pandemic Questionnaire, the TIS and the PCL-5.

After completing the items on sociodemographic information and availability of PPE, participants were directed to the following three self-report questionnaires. The first assessed traumatic experiences regarding the COVID-19 pandemic. At the end of the COVID-19 traumatic events questionnaire, participants had to indicate the event that they considered to be the most traumatic (index trauma) and answer the PCL-5 and TIS based on this event.

Participants took approximately 15 minutes to complete all the questionnaires and submit their answers. After submitting their answers, the participants were presented with a text that contained supportive information on how to cope with the psychological impact of the COVID-19 pandemic and a list of professional support contacts in case they needed psychological help.

2.6 Statistical analysis

Proportions were calculated for age, gender, ethnic group, income, professional level, institution, PPE availability and worst traumatic COVID-19 experiences. Means and standard deviations were calculated for the TI and PTSS scores. This information is shown in Table 1.

To investigate whether age, gender, PPE availability and worst traumatic COVID-19 experiences influenced our variables of interest, i.e., TI (independent variable) and PTSS scores (dependent variable), we conducted a Mann-Whitney test and the Kruskal-Wallis test. Variables significantly related to the TI and PTSS scores were included as potential confounders in the multiple regression models. Nonparametric tests were chosen as the visual inspection of the frequency distribution (histograms) and normal Q-Q plots (quantile-quantile plot) of the raw data within each level of the groups, and of residuals for linear models,

indicated deviation from normality. In addition, p-values for the Shapiro-Wilk test for each group, for both raw data and residuals, were below 0.05 and equality of variances assessed by Levene's test suggest heteroscedastic results except for gender (PCL-5 p=0.34; TIS p=0.11) and age (TIS p= 0.11).

Because the psychometric instruments used to measure our outcome (PCL-5) and our main predictor variable (TIS) were applied online, i.e., a different mode from the validated version of the scales, we ran a confirmatory factor analysis (CFA) to examine the construct factorial validity of the PCL-5 and TIS for the present sample. Additionally, we ran a multiple group CFA to detect if healthcare workers interpreted the PCL-5 scale and TIS differently according to gender, age, PPE availability or worst traumatic COVID-19 experiences. We examined measurement invariance at the configural, metric and scalar levels. The scripts used (see Appendix II) and the results of these analyses are presented in the supplemental material.

2.6.1 Association between TI and PTSS severity

We performed a multivariate negative binomial regression in the full sample to examine the influence of TI scores in predicting PTSS scores. Normality tests were carried out to investigate the distribution profile of the dependent variable for the full sample data. The Shapiro-Wilk test indicated that the dependent variable, i.e., PCL-5 scores, and the residuals for linear models did not follow a normal distribution (W=0.95 p<0.001; W=0.99 p<0.001 respectively). Additionally, a scatterplot of the residuals suggests that the data are not homoscedastic. Overdispersion was detected by the Cameron and Triverdi (CT) test for overdispersion. A Lambda t test score of 17.338 and p-value of < 0.001 were obtained from R using the overdisp () function of the overdisp package (Freitas Souza et. al, 2020). We also checked the deviance divided by its degrees of freedom for the poisson model and the ratio was 7.2, also indicating overdispersion. The likelihood-ratio test of alpha=0 (dispersion parameter), obtained using "nbreg" command in stata, was significantly different from zero (p<0.001) suggesting that a negative binomial model was probably better than a poisson model. Thus, a negative binomial model was chosen to address the problem of overdispersed data and nonnormality conditions. The exponentiated regression coefficients provide the incidence ratio rate (IRR), which is interpreted as an increase or decrease in the dependent variable in terms of the percentage for each unit change in the independent variable. Both data were entered as continuous variables. Potential confounders investigated in the previous analysis, such as age, gender, PPE availability and worst traumatic COVID-19 experiences, were included in the multivariate model, as they showed significant associations with the variables of interest, i.e., TI (independent variable) and PTSS (dependent variable) scores. Participants opting not to declare if PPE was available or not (n=21) were not included in any analysis involving this confounding variable. Thus, the final sample for this analysis included 980 participants.

2.6.2 TI as risk factor for PTSD diagnosis

A logistic regression model was selected to investigate whether high levels of TI scores would represent an increased chance of presenting high levels of PTSS symptoms compatible with a PTSD diagnosis. For this analysis, we excluded participants who reported an index trauma occurring within less than 30 days, as according to the DSM-5 criteria for PTSD diagnosis, symptoms must last for more than a month. A total of 509 participants reported an index trauma event that occurred within more than 30 days. Probable PTSD was added as a dichotomous variable (Yes or No). Classification of the presence of a high level of symptoms was based on a cutoff score of 36 points or higher on the PCL-5, which the literature suggests shows the best diagnostic performance for predicting a diagnosis of PTSD (Pereira-Lima et al., 2019). Thus, with this analysis we investigated if high levels of tonic immobility would increase the risk of being classified in the group in which the degree of PTSD symptoms is above the criteria for PTSD diagnosis. Tonic immobility was also included as a dichotomous variable with "low TI" and "high TI" groups created by median split. Age, gender, PPE availability and worst traumatic COVID-19 experiences were also included in the final logistic regression model as potential confounders. Participants opting not to declare if PPE was available or not were not included (n=10). Thus, for this analysis, the final sample consisted of 499 participants.

Mann-Whitney and Kruskal-Wallis tests were conducted using Statistica 12.0. SPSS to calculate internal consistency and logistic regression. CFA and multigroup CFA were performed with Lavaan (an R program). Negative binomial regression was run with Stata 12.0. Statistical significance was established at p<0.05 for all analyses.

3. Results

The full sample of 1001 participants was included for further analysis, and Table 1 (full sample column) provides sociodemographic information, including frequencies of age, gender, ethnic group, income, professional level, type of institution (public, private or both), PPE availability and worst traumatic COVID-19 experiences. Additionally, scores for tonic immobility and PTSD symptomatology are also provided.

The sample was mostly female (76.4%), white (65.2%) and aged between 18 and 39 years old (51.9%). More than 80% of our sample reported a higher professional level, and 45% of our sample had income ranging from five to ten times the minimum wage. Fifty-three percent of participants stated that they worked in a public institution, and more than 48% declared inconstant or unsatisfactory PPE availability. Additionally, the COVID-19 index trauma that was more frequently reported was "learning through others about the death of a family member or a coworker due to COVID-19", followed by "experiencing the imminent risk of death of a family member or coworker due to COVID-19", as reported by 25.5% of the sample and 18.6% of the sample, respectively.

The mean score for tonic immobility was 14.8 for the full sample (n =1001) and 14.4 for the sample reporting an index trauma event within more than 30 days (n = 509). "Low TI" calculated from the median split procedure presented a mean score of 5.9. Notably, "high TI" presented a TI score of 23.5, i.e., in the upper half of the scale range. Further, we explored the

percentage of participants with scores above the criteria, which are proposed in the literature (Heidt et al., 2005; Fusé et al., 2007) to serve as evidence of the occurrence of a significant immobility reaction, i.e., scores above the midpoint of the range of the TI scale. Fusé et al (2007) also suggested that scoring at or above 28 was evidence of extreme TI reaction, a cutoff value representing approximately the upper third range of the TI scale version (range 0-42) used by them. Considering the six-item version employed in this study (range 0-36), scores equal to or higher than 18 might be considered suggestive of significant immobility occurrence. In our sample, 412 participants (41%) met the criteria for significant immobility reaction. Additionally, 192 (19%) participants presented TI scores in the upper third of the scale range (> 24), suggesting extreme levels of tonic immobility.

Table 1: Sample characteristics for the full sample and for the group of participants presenting more than 30 days after the traumatic experience

| | Full sample | | Trauma | >30 days | | |
|---|-------------|-----|--------|----------|--|--|
| 9 | n | % | n | % | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | 20 | • • | ~~ | | | |

Gender

Professional level

D. 1

Personal protective

Worst traumatic COVID-19 experience (index trauma)

| Personally witnessing | 145 | 14.5 | 57 | 11.2 |
|---|-----|------|-----|------|
| Personally witnessing family members or coworkers dving | 51 | 5.1 | 32 | 6.3 |
| Hearing through others of a | 255 | 25.5 | 137 | 26.9 |
| Experiencing a family | 186 | 18.6 | 94 | 18.5 |
| Being exposed to patients | 120 | 12.0 | 52 | 10.2 |
| Being contaminated with the | 92 | 9.2 | 57 | 11.2 |

| | Being afraid of having | 152 | 15.2 | 80 | 15.7 |
|------------------------|------------------------|-------|---------------|-------|---------------|
| | | n (%) | Mean | n (%) | Mean |
| Tonic immobility score | | 1001 | 14.8 | 509 | 14.4 |
| | High score | 507 | 23.5 (6.1) | 260 | 23.0 (6.4) |
| | Low score | 494 | 5.9 | 249 | 5.3 |
| Posttraumatic stress | | 1001 | 25.3 | 509 | 24.2 |
| Posttraumatic stress | | 256 | 49.23 | 121 | 49.08 |

3.1. Gender, age, PPE availability and traumatic experiences associated with tonic immobility and PTSD scores

Our main focus was to investigate whether tonic immobility would be associated with PTSS severity in the pandemic context, even when we controlled for potential confounders. First, we checked whether variables commonly related to PTSS in the literature, such as age, gender, PPE availability and worst traumatic experience, could also influence TI and PTSS scores. Table 2 shows the results of the Mann-Whitney and Kruskal-Wallis tests used to determine whether these variables were systematically related to tonic immobility and PTSD scores. The main effects results show that all variables significantly influenced tonic immobility and PTSS scores (all p<0.01). Tonic immobility and PTSS scores were significantly higher for younger groups (18-29 years and 30-39 years) than older groups (tonic immobility: H=23.54, p-value<0.001; PTSD: H=20.52, p-value<0.001), for women than men (tonic immobility: U=66809.00, p-value=0.000; PTSD: U=69815.50, pvalue=<0.001), and for those with inconstant/unsatisfactory PPE availability than those with satisfactory availability (tonic immobility: U=100323.5, p-value<0.001; PTSD: U=93618.00, p-value<0.001). For the variable worst traumatic COVID-19 experience, significantly higher tonic immobility and PTSD scores were obtained for those who reported "being afraid of having contaminated someone close to them" (tonic immobility: H=19.79, p-value=0.003; PTSD: H=25.79, p-value<0.001). However, it is important to mention that the mean comparisons of TI scores across index trauma groups must be considered with caution, as only partial scalar invariance was supported for the TI scale across these groups (see the supplemental material).

Table 2: Group differences for tonic immobility and PTSD scores

| | Tonic immobility score | | | | | PTSD score | | | | |
|---------------------------|------------------------|----------|----------------|-------------|---------------------------------|------------------------|----------|----------------|-------------|---------------------------------|
| | Media n by group | IQ R | Main effect | p- value | Effec t size Cohe n d* | Media n by group | IQ R | Main effect | p- value | Effec t size Cohe n d* |
| Age – years, mean (SE) | | | | | | S | C | Ö, | | |
| 18-29 years | 17.0 | 16. 0 | H=23.54 | <0.00 | 0.278 | 25.0 | 25. 0 | H=20.2 5 | <0.00 | 0.255 |
| 30-39 years | 15.0 | 17. 0 | | >5 | | 23.0 | 27. 0 | | | |
| 40-49 years | 12.0 | 16. 5 | 9 | | | 20.5 | 21. 5 | | | |
| 50-59 years | 12.0 | 18. 0 | | | | 20.0 | 22. 0 | | | |
| 60 or more years | 10.0 | 14. 0 | | | | 16.0 | 22. 5 | | | |
| Gender | | | | | | | | | | |
| Female | 16.0 | 17. 0 | U=6680 9 | <0.00 1 | 0.387 | 23.0 | 24. 0 | U=6981 5 | <0.00 1 | 0.324 |
| Male | 8.0 | 14. 5 | | | | 16.0 | 22. 0 | | | |

| Personal protective |
|---------------------|
| equipment (PPE) |
| availability |

Being exposed to patients severely infected with the

disease

13

15. 0

| Satisfactory | 12 | 16. 0 | U=1003 23 | <0.00 1 | 0.282 | 18 | 21. 0 | U=9361 8 | <0.00 1 | 0.387 |
|---|----|----------|--------------|------------|-------|----|----------|-------------|------------|-------|
| Inconstant/Unsatisfact ory | 17 | 18. 0 | | | | 26 | 28. 0 | * | | |
| Worst traumatic COVID-19 experiences (index trauma) | | | | | | O | C | | | |
| Personally witnessing patients dying of the disease | 13 | 17. 0 | H=19.79 | 0.003 | 0.238 | 18 | 20. | H=25.7 9 | <0.00 1 | 0.278 |
| Personally witnessing family members or coworkers dying of the disease | 17 | 18. 0 | 9 | | | 23 | 20. | | | |
| Hearing through others of a family member or co-worker dying of the disease | 13 | 19. 0 | | | | 21 | 22. | | | |
| Experiencing a family member or coworker suffering an imminent risk of death due to the disease | 12 | 16. 0 | | | | 22 | 24. | | | |

25. 5

23

| Being contaminated with the disease | 15.5 | 20. 5 | 18.5 | 26. 0 |
|--|------|----------|------|----------|
| Being afraid of having contaminated someone close to you | 18.5 | 16. 0 | 29 | 30. 0 |

Notes: IQR - interquartile range; *Cohen d - Lenhard, W. & Lenhard, A. (2016). Computation of effect sizes. Retrieved from https://www.psychometrica.de/effect_size.html. Psychometrica. DOI: 10.13140/RG.2.2.17823.92329

3.2. Association between TI and PTSS severity

Multivariate negative binomial regression was run to test whether tonic immobility was related to PTSS severity in the full sample. Table 3 presents the results of this analysis. Tonic immobility was significantly associated with the PTSS level [IRR=1.044 (CI 1.04-1.05); p<0.000], meaning that each unit increase in tonic immobility was associated with an increase in the PTSD symptoms score by a factor of 1.044, i.e., representing an increase of 4.4% in the mean PTSD symptoms score. When the potential confounders age, gender, PPE availability and worst COVID-19 trauma were also included in the model, the association remained statistically significant, highlighting the relevance of tonic immobility for PTSS severity [IRR=1.043 (CI 1.04-1.05); p<0.001]. This result means that when potential confounders were included in the model, if a participant was to increase his TI score by one point, his PCL score would be expected to increase 4.3%. Figure 2 depicts the raw and adjusted values of the IRR obtained from the multivariate model. Notably, the impact of tonic immobility remained stable during all steps of model adjustment.

Additionally, we run a multivariate negative binomial regression to test whether items more strictly related to the motor aspects of the tonic immobility reaction were related to PTSD severity. In this analysis, items from the six-item version of the TI scale that assess other reactions, such as fear and dissociation, were not included. We conducted this analysis to test whether the more "strict motor" aspects of the tonic immobility response were associated with PTSD symptoms severity. As described in the supplemental material, the results are very similar when only the four motor items are included in the models, reinforcing the idea that the immobility aspect is crucial to the results reported in the present study.

Table 3: Multivariate negative binomial regression for the prediction of PTSD severity

| | Mu | ltivariate analy | sis | | |
|---|-----|------------------|---------|--------|---------|
| β | IRR | Wald chi- | Pseudo- | 95% CI | p-value |

| | | | square | R2 | | |
|---|----------|--------|---------|------|---------------|--------|
| | | | | | | |
| Models | | | | | | |
| | | | | | | |
| Step 1 | 0.0043 | 1.0444 | 480.486 | 0.05 | [1.04 - 1.05] | <0.001 |
| | | | | | . , | |
| Not a dimeta d | | | | | | |
| Not adjusted | | | | | | |
| | | | | | | |
| Step 2 | 0.0043 | 1.0437 | 458.816 | 0.05 | [1.04 - 1.05] | <0.001 |
| | | | | | | |
| Adjusted for age | | | | | | |
| | | | | | | |
| Step 3 | 0.0042 | 1.0431 | 439,741 | 0.05 | [1.04 - 1.05] | <0.001 |
| | | | 10 | | | |
| Adjusted for age and | | | | | | |
| gender | | | | | | |
| | | | * | | | |
| Step 4 | 0.0042 | 1.0425 | 413.309 | 0.05 | [1.04 - 1.05] | <0.001 |
| | | | | | | |
| Adjusted for age and | | | | | | |
| gender plus PPE availability |) | | | | | |
| avanability | | | | | | |
| | | | | | | |
| Step 5 | 0.0041 | 1.0425 | 404.01 | 0.06 | [1.04 - 1.05] | <0.001 |
| | | | | | | |
| Final model | | | | | | |
| Adjusted for age, gender | | | | | | |
| and PPE availability plus worst COVID-19 trauma | | | | | | |
| | | | | | | |

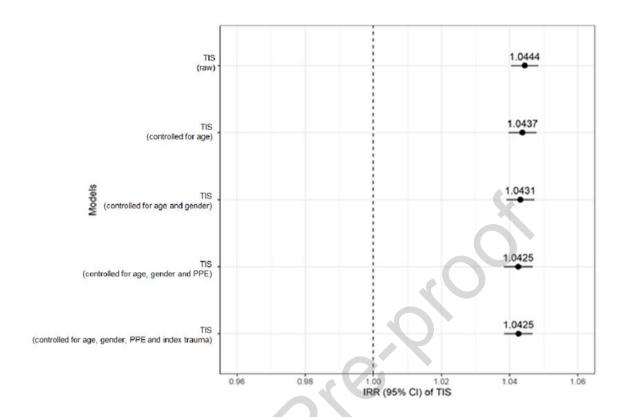


Figure 2: Incidence rate ratio - IRR - (with 95% confidence interval) obtained from the multivariate negative binomial regression model exploring the association between TI and PTSS severity. The figure depicts the raw and adjusted models (adjusted for age, gender, PPE availability and worst trauma experiences). Notably, the impact of tonic immobility remained stable during all steps of model adjustment.

3.3. TI as a risk factor for PTSD diagnosis

Here, we used logistic regression analysis to explore how tonic immobility impacted the probability of presenting a level of PTSD symptoms compatible with PTSD diagnosis. Only participants presenting more than 30 days after the traumatic experience were included in the model. For the purpose of this analysis, TI was included as a dichotomous variable, and the groups (low TI versus high TI) were divided based on a median split procedure. We also tested if applying different criteria, specifically those proposed in the literature (Heidt et al., 2005; Fusé et al., 2007) as evidence of the occurrence of a significant (equal or above the midpoint range of the scale) or extreme immobility reaction (upper third of the scale range) would ensure similar results (see the supplemental material for details and results). The PCL-5 score was also treated as a dichotomous variable, and participants were designated to the present (n=121) or absent (n=388) PTSD group based on a cutoff point of 36 or higher (Pereira-Lima et al., 2019).

Table 4 shows the results of the raw and adjusted models. Age, gender, PPE availability and worst COVID-19 trauma were included as potential confounders. The results show that in the raw model, high levels of tonic immobility increased the chances of having a probable diagnosis of PTSD by 9.09 times (OR=9.09, 95% CI=5.24-15.79, p-value<0.001). After confounders were controlled, the results were comparable. The adjusted model showed that high levels of tonic immobility were associated with a 9.08-fold increase in the probability of having a probable diagnosis of PTSD (OR=9.08, 95% CI=5.06-16.31, p-value>0.001). Figure 3 depicts the odds ratio of the raw and adjusted multiple regression model.

Additionally, we ran a logistic regression to assess whether items more strictly related to the motor aspects of the tonic immobility reaction also impacted the probability of presenting a level of PTSD symptoms compatible with PTSD diagnosis. Results show that in the raw model, high levels of the strict motor tonic immobility increased the chances of having a probable diagnosis of PTSD by approximately 8 times (OR=7.97, 95% CI=4.64-13.67, p value<0.001), and this remained roughly the same after controlling for confounders (OR=7.75, 95% CI=4.37-13.73, p value<0.001). More details of the analysis and results are presented in the supplementary material.

Table 4: Logistic regression results of the raw and adjusted models.

| | Tonic immobility odds ratio for PTSD | | | | | | | | |
|------------------------------------|--------------------------------------|-------|---------------------|---------------|--------------|---------|--|--|--|
| | β | OR | Wald chi- square | Pseudo- R2 | 95% CI | p-value | | | |
| Models | | | | | | | | | |
| Step 1 Not adjusted | | | | | | | | | |
| Low TI | Ref. | | | | | | | | |
| High TI | 2.208 | 9.098 | 61.591 | 0.15 | 5.242-15.792 | <0.001 | | | |
| Step 2 Adjusted for age | | | | | | | | | |
| Low TI . | Ref | | | | | | | | |
| High TI | 2.171 | 8.765 | 58.905 | 0.17 | 5.035-15.259 | <0.001 | | | |
| | | | | | | | | | |
| Step 3 Adjusted for age and gender | | | | | | | | | |
| Low TI . | Ref | | | | | | | | |

| High TI | 2.170 | 8.754 | 58.238 | 0.17 | 5.015-15.283 <0.001 |
|--|-------|-------|--------|------|-------------------------------|
| | | | | | |
| Ston 4 | | | | | |
| Step 4 Adjusted for age and gender plus PPE availability | | | | | |
| Low TI | Ref. | | | | |
| High TI | 2.173 | 8.783 | 54.674 | 0.20 | 4.938-15.623 <0.001 |

Step 5 -Final model

Adjusted for age, gender and PPE availability plus worst COVID-19 trauma

Low TI Ref.

High TI 2.206 9.081 54.555 0.22 5.057-16.308 **<0.001**

Note: Pseudo-R2 is the McFadden's pseudo R-squared

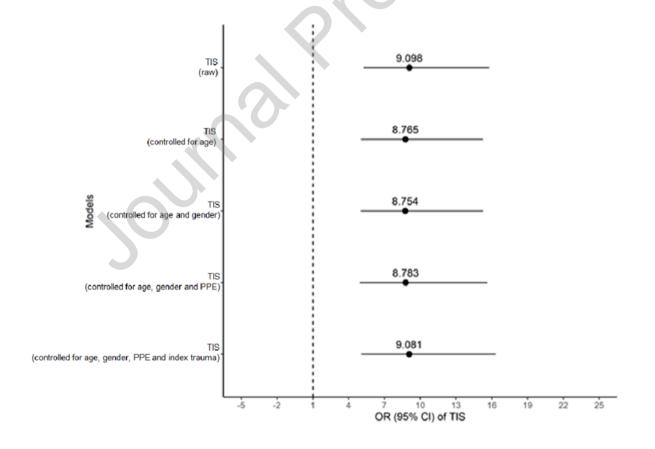


Figure 3: Odds ratio (with 95% confidence interval) obtained in the logistic regression model. The figure depicts the raw and adjusted models (adjusted for age, gender, PPE availability and worst trauma experiences). Notably, high tonic immobility increased the chances of having a probable diagnosis of PTSD by 9.09 times; this result did not change after confounders were controlled.

4. Discussion

The goal of the present study was to investigate whether the overwhelming and inescapable threat imposed by the pandemic context would evoke the defensive tonic immobility response in HCWs during traumatic events related to COVID-19 and to investigate if it represents a vulnerability factor for PTSD. Our main results suggest that a significant tonic immobility reaction (equal to or above the midpoint range of the scale) was reported to occur during traumatic events related to the COVID-19 pandemic by 41% of HCW, with 19% of the sample reaching very high scores of TI. Additionally, this peritraumatic response was significantly associated with PTSS severity and higher chances of PTSD diagnosis, even after potential confounders (age, gender, PPE availability and worst traumatic COVID-19-related experience) were controlled. The results remain very similar when using a more strictly "motor version" (the four-item motor subscale used by Rocha-Rego et al. (2009)) or the TI scale (see the supplemental material for details).

4.1. TI in the pandemic context

To the best of our knowledge, this research is the first study to explore the occurrence of tonic immobility during traumas related to a pandemic context in HCW. In the literature, this defensive response in humans is more commonly described as occurring during interpersonal violence situations, such as sexual violence or armed robbery (Galliano et al., 1993; Bovin et al., 2008; Humphreys et al., 2010). Here, we have expanded the knowledge about traumatic experiences that could serve as triggers for this type of defensive response by showing its occurrence in healthcare workers during trauma related to COVID-19. It is also important to highlight that the level of TI reported by HCW was similar to the TI scores described in the literature for sexual violence trauma. Using the same 6-item version of the TIS, Kalaf et al. (2017) investigated TI occurrence during different types of traumatic events and reported that the highest scores were obtained for childhood sexual abuse and adult sexual abuse, with mean TI scores of 16.7 and 21.5, respectively. In the present study, the mean tonic immobility score for the whole sample was 14.8, reaching a mean score of 23.5 in the high tonic immobility group. Nonetheless, these comparisons to the literature must be carefully interpreted, as the factorial invariance of the measurement made across the samples was not assessed. Additionally, according to the criteria proposed in previous studies (Heidt et al., 2005; Fusé et al., 2007), 41% of our sample had scores above the midpoint range of the scale being compatible with significant immobility reactions and 19% of the participants presented TI scores suggestive of extreme levels of tonic immobility, i.e., in the upper third of the scale range (Fusé et al., 2007).

The high levels of tonic immobility reported here emphasize the need to assess the occurrence of this response during pandemic contexts, when many situations might be perceived as an overwhelming and inescapable threat to healthcare workers. These are salient elements associated with the induction of tonic immobility in nonhuman animals. As pointed out by Marx et al. (2008), due to human cognitive/symbolic representation capabilities, a wide range of stimuli and contexts might be suggestive of restraint or inescapability, and the perception of what is frightening may be highly influenced by other factors, such as previous experiences (Foa & Kozak, 1986), leading to an escalation in the defensive response cascade with exposure to danger cues (Alves et al., 2014). Identifying traumatic situations that might evoke tonic immobility in humans is extremely important, as the occurrence of this peritraumatic response has been associated with mental health impairments, e.g., greater risk for more severe PTSD symptomatology.

4.2. Tonic immobility and psychopathology

Our data add to the literature by showing that the peritraumatic TI prompted by COVID-19 traumatic events was significantly associated with PTSD symptom severity and with an increased risk for PTSD diagnosis in a HCW sample. Each unit increase in the TI score was associated with a 4.4% increase in the PCL-5 score, and the high TI group had a 9.09 times greater chance of having a PTSS score compatible with a PTSD diagnosis. These results are in accordance with previous studies from our group reporting an association between tonic immobility and PTSD symptom severity, poor response to pharmacological treatment and poor prognosis in clinical and nonclinical samples (Rocha-Rego et al., 2009; Fiszman et al., 2008; Portugal et al., 2012; Lima et al., 2010; Maia et al., 2015; Kalaf et al., 2015; Volchan et al., 2017; Magalhães et al., 2021). Studies from other groups have also described the implications of tonic immobility on mental health, showing that the tonic immobility response is a factor that increases individuals' vulnerability to PTSD development (Bovin et al., 2008; Heidt et al., 2005; Humphreys et al., 2010) and could impair PTSD recovery (Hagenaars & Hagenaars, 2020). In the same vein, Moller et al. (2017) showed that the occurrence of tonic immobility seems to increase the risk of PTSD prevalence after sexual assault by 2.75 times. Taken together, these results reveal that tonic immobility in the pandemic context seemed to be as harmful as other traumatic situations more commonly associated with this response, representing an important risk factor for PTSD in healthcare professionals.

The exact relation between TI and PTSD symptomatology is not known, but studies have raised some hypotheses of potential mechanisms. Marx et al. (2008), taking into account that 47% of a sample of rape survivors who experienced TI reported these symptoms to be extremely frightening, speculated that the experience of TI itself, rather than the trauma itself, might be so aversive that it directly influences the development of PTSD symptoms. A study by Bovin et al. (2008) suggests that TI is a mediator of the relationship between fear, perceived inescapability, and PTSD symptoms. Another important aspect is the fact that TI might contribute to feelings of self-blame and guilt for not reacting as expected (Suarez & Gallup, 1979; Marx et al., 2008; Mezey and Taylor, 1988; Fusé et al., 2007). Thus, TI

occurrence might elicit negative cognition and is associated with feelings of uncontrollability and inescapability, which are considered to be relevant elements for the etiology of PTSD (Foa et al., 1992). These overwhelming feelings may alter the processing of trauma information, leading to a poorly elaborated trauma memory that is incongruous with the ordinary autobiographical memory system and thus involuntarily triggered by perceptual cues and contaminated with sensory traces of the trauma (Brewin, Dalgleish, & Joseph, 1996). Moreover, according to the cognitive model of PTSD (Ehlers and Clark, 2000), negative appraisals of the way one behaved during a traumatic event (such as the absence of expected reaction) might be an important process associated with the development and persistence of PTSD. Highlighting the reflexive and involuntary nature of TI and revealing the variety of traumatic situations that can evoke this response are urgent tasks.

4.3. Traumatic events related to COVID-19 pandemics

Since the beginning of the COVID-19 pandemic, a wide number of stressful COVID-19 experiences have been listed in different published papers, and PTSD symptoms have been addressed. However, in most studies, self-reported symptoms were accessed without anchoring to DSM-5 criterion A for PTSD (Di Tella et al., 2020; Robles et al., 2020; Blekas et al, 2020; Dosil et al., 2020), and many COVID-19 experiences might not qualify as a DSM-5-defined traumatic event. Anchoring PTSD self-report symptom assessment to a target event is essential (Van Overmeire, 2020), as assessments without proper anchoring to a criteria A event might only be interpreted as an indication of levels of general distress (Asmond & Taylor, 2021). To be meet criteria A for PTSD diagnosis, an event must involve actual or a possible threat of death or serious injury. Trauma exposure might be directly experienced or witnessed or learned of occurring to a close loved one or involve repeated exposure to aversive details of it, usually due to professional duties. Since an large number of scientific papers addressing COVID-19-related PTSD erroneously apply DSM-5 PTSD criteria A (the definition of a potentially traumatic event (Asmundson & Taylor, 2021), an important strength of the present study is its assessment of traumatic events specifically related to the COVID-19 pandemic and in accordance with DSM-5 criteria A for the diagnosis of PTSD. This approach is important in contributing to more homogeneous PTSDrelated research, leading to better comprehension of the disorder, which in turn may guide researchers to better treatment possibilities (Asmundson & Taylor, 2021; Norrholm et al., 2021).

The traumatic experience related to COVID-19 most frequently reported was "learning, through others, about the death of a family member or a coworker due to COVID-19." This finding is in line with the literature about trauma prevalence before the pandemic, as trauma related to death of a loved one has been reported as the most frequent trauma (Luz et al., 2016). The experience of "believing or having confirmation that one may have transmitted the virus to someone very close (coworker, partner, friend or family)" presented the highest PTSD symptom scores in comparison to the other traumatic experiences. As shown by Cotrin et al. (2020), more than 95% of healthcare workers reported changes in

habits due to a fear of contaminating family members. The fear of contaminating family members might be related to stress experienced by HCW (Walton et al., 2020).

4.4. Associated factors related to PTSD symptomatology

Scores for tonic immobility and PTSD were significantly higher for younger groups than for older groups, for females and for those who reported that PPE was distributed inconsistently or unsatisfactorily. These results are in agreement with scientific literature showing that young professionals (Cai et al., 2020; Zhang et al., 2020; Robles et al., 2020) and females (Benfante et al., 2020; Di Tella et al., 2020; Dosil et al., 2020; Blekas et al., 2020) were at a greater risk of developing several psychological problems during the COVID-19 pandemic. Younger professionals tend to have less work experience and hence face a diminished sense of self-efficacy at work, putting this group in a more vulnerable position after trauma. Furthermore, gender barriers to women's progress in the workplace due to gender inequalities and the burden of care responsibilities faced by women have a negative impact on mental health (Xue & McMunn, 2021; Gupta et al., 2019). Finally, the scarcity of PPE can lead to a fear of contamination, the possibility of experiencing a severe course of the disease and/or imminent death and the recognition of oneself as a threat to the lives of other people. These experiences have been common during the pandemic and have possibly contributed to an accumulation of traumatic events, which represents a risk factor for the development of PTSD (Pfefferbaum & North, 2021; Sekowski et al., 2021).

4.5. Limitations

There were some limitations to the study. This was a cross-sectional study, and the retrospective design may have led to recall bias. Data were obtained by a convenience snowball sampling technique through a link sent via WhatsApp and e-mail, which did not guarantee sample representativeness. To minimize this issue, major health worker groups were contacted to publicize the project and the survey on websites and their social media. Additionally, the study was conducted as a web survey including only self-report questionnaires. Therefore, it is not possible to affirm that participants correctly understood the questions and to confirm the reliability of their responses. Furthermore, participants' responses might have been affected by social desirability. Although the study design did not guarantee sample representativeness, online self-report measures seemed to be the most appropriate due to the challenging circumstance imposed by the pandemic context. Selection bias for location and gender might have occurred. The southeastern region of Brazil was overrepresented (74.1%) in our sample, while the northern regions, where the worst consequences of COVID-19 on the mental health of HCW could have occurred, were less represented (15.9%) (Ribeiro et al., 2020). In addition, the reported gender differences should be interpreted cautiously, as women were overrepresented in the study (76.4%). However, this seems to be similar across different studies (Dosil et al., 2020) and in healthcare scenarios globally (CONASEMS, 2020). Finally, it is important to mention that some aspects of this study followed an exploratory approach, e.g., the inclusion of PPE availability and worst traumatic COVID-19 experiences in the models as potential confounders for the association between TI and PTSD. Thus, future studies using confirmatory approaches are necessary to confirm these findings.

4.6. Conclusions

The present study expanded the scope of previous research on peritraumatic tonic immobility by showing that this defensive behavior was also present during pandemic-related traumatic situations in a sample of healthcare workers. Furthermore, our results showed that tonic immobility could predict significantly higher symptomatology of PTSD and an increased probability of presenting a PTSD diagnosis. These findings show that it is extremely important to direct attention to the population of HCW and implement strategies that might attenuate the risk factors for PTSD present in their professional and personal environments. It might be particularly helpful if elements that are essential to prompt tonic immobility, i.e., elements favoring a situation to be perceived as an overwhelming and inescapable threat, are reduced. Adequate provision of PPE and appropriate professional training are examples of actions that might reduce risk perception in these professionals. Additionally, tonic immobility occurrence should be screened, and psychoeducation about its reflexive biological nature should be introduced to reduce the feelings of guilt and shame that might accompany this defensive reaction (Moller et al., 2017). Finally, psychological and psychiatric treatment should continue to be offered to healthcare professionals with intense workloads (Chen et al., 2020).

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Highlights

- The peritraumatic TI reaction was reported for COVID-19 traumatic events.
- TI during COVID-19 traumatic events was associated with increased severity in PTSS.
- High TI scores in HCW were associated with higher odds of a PTSD diagnosis.